

AMENDMENTS TO THE CLAIMS

1. (Original) A method of characterizing the biological activity of a candidate compound comprising:

placing one or more cells into an area of observation in a sample well;

exposing said one or more cells to said compound;

repetitively exposing said one or more cells to a series of biphasic electric fields at a rate of approximately 20 to 100 pulses per second, wherein said electric fields exhibit limited spatial variation in intensity in the area of observation of less than about 25% from a mean intensity in that area, and wherein said electric fields produce a controlled change in transmembrane potential of said one or more cells; and

monitoring changes in the transmembrane potential of said one or more cells by detecting fluorescence emission of a FRET based voltage sensor from an area of observation containing said one or more cells.

2. (Original) The method of Claim 1, wherein said one or more electrical fields cause an ion channel of interest to open.

3. (Original) The method of Claim 1, wherein said one or more electrical fields cause an ion channel of interest to be released from inactivation.

4. (Original) The method of Claim 1, wherein said one or more cells comprise a voltage regulated ion channel.

5. (Original) The method of Claim 4, wherein said voltage regulated ion channel is selected from the group consisting of a potassium channel, a calcium channel, a chloride channel and a sodium channel.

6. (Original) The method of Claim 1, wherein said one or more electrical fields varies over an area of observation by no more than about 15 % from the mean electrical field at any one time.

7. (Original) The method of Claim 6, wherein said one or more electrical fields varies over an area of observation by no more than about 5 % from the mean electrical field at any one time.

8. (Original) The method of Claim 1, wherein said one or more electrical fields are selected from a square wave-form, a sinusoidal wave-form or a saw tooth wave-form.

9. (New) A method for modulating the voltage dependent state of an ion channel by modulating the transmembrane potential of said cell comprising: repetitively applying biphasic electric field pulses to said cell, wherein said pulses have a maximum amplitude of less than approximately 90 V/cm, wherein said pulses are applied at a rate of at least about 1 per second, and wherein the total duration of each pulse is at least about 1 millisecond.

10. (New) The method of claim 9 wherein said biphasic electric field is a square wave kernel of about 5 msec per phase.

11. (New) The method of claim 9 wherein said pulses have a maximum amplitude of about 25 V/cm.

12. (New) The method of claim 9 wherein said pulses are applied at a rate of about 20 per second.

13. (New) The method of claim 9 wherein said total duration of about three seconds.

14. (New) A method of assaying a compound for voltage-dependent blocking activity against a target ion channel comprising:

a. selecting a cell line having a normal resting transmembrane potential corresponding to a selected voltage dependent state of said target ion channel;

b. expressing said target ion channel in a population of cells of said selected cell line;

c. exposing said population of cells to said compound;

d. repetitively applying biphasic electric field pulses to said population of cells, wherein said pulses have a maximum amplitude of less than approximately 90 V/cm, wherein said pulses are applied at a rate of at least about 1 per second, and wherein the total duration of each pulse is at least about 1 millisecond so as to effect a controlled change in the transmembrane potential of said population of cells; and

e. monitoring changes in the transmembrane potential of said population of cells.

15. (New) The method of claim 14, wherein said target ion channel is exogenously expressed in said cell line.

16. (New) The method of claim 14, wherein said cell line is transfected with nucleic acid encoding said target ion channel.

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17. (New) The method of claim 16, wherein said cell line expresses insignificant levels of other ion channels.

18. (New) The method of claim 17, wherein said cell line is selected from the group consisting of CHL, LTK(-), and CHO-K1.

19. (New) The method of claim 14 wherein said biphasic electric field is a square wave kernel of about 5 msec per phase.

20. (New) The method of claim 14 wherein said pulses have a maximum amplitude of about 25 V/cm.

21. (New) The method of claim 14 wherein said pulses are applied at a rate of about 20 per second.

22. (New) The method of claim 14 wherein said total duration of about three seconds.

23. (New) The method of claim 14, wherein exposing said population of cells to said compound is performed before applying said electric field pulses.

24. (New) The method of claim 14, wherein applying said electric field pulses is performed before exposing said population of cells to said compound.

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